UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,964	12/07/2005	David L. Keefe	59802(49947)	8976

21874 7590 12/10/2008

EDWARDS ANGELL PALMER & DODGE LLP
P.O. BOX 55874
BOSTON, MA 02205

EXAMINER	
JOHANNSEN, DIANA B	
ART UNIT	PAPER NUMBER
1634	
MAIL DATE	DELIVERY MODE
12/10/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/531,964	KEEFE, DAVID L.	
	Examiner	Art Unit	
	Diana B. Johannsen	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 13-53* is/are pending in the application.

4a) Of the above claim(s) *51-53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 13-50* is/are rejected.

7)☒ Claim(s) *32-33* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 April 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *0405;0905*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The instant application is a 371 of PCT/US03/32672, filed October 13, 2003. The international search report for PCT/US03/32672 has been received and considered. It is also noted that the amendments to the specification filed April 19, 2005 (updating the first line of the specification) and May 5, 2008 (adding SEQ ID NOS to the specification) have been reviewed and entered. The sequence listing filed May 5, 2008 has also been entered.

2. The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 41-54 have been renumbered as claims 40-53 (it is noted that applicant's claim set does not include a claim corresponding to the number 40). Renumbered claims 43-45 have thus been treated as dependent on renumbered independent claim 42, renumbered claim 47 has been treated as dependent on renumbered claim 46, and renumbered claims 48-50 have been treated as dependent on renumbered claim 47. It is noted that the required correction in numbering should be reflected in any amendment filed in reply to this Office action.

Election/Restrictions

4. Applicant's election without traverse of Group I, claims 1-8 and 13-51, and of SEQ ID NO: 1, in the reply filed on September 3, 2008 is acknowledged. It is noted that

the correct numbers of the elected claims (after correction of the misnumbering noted above) are claims 1-8 and 13-50.

5. Claims 51-53, as well as the non-elected SEQ ID NOs encompassed by Group I (SEQ ID NOS 2-10; see text of claims 48-50), are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on September 3, 2008.

Information Disclosure Statement

6. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

7. The information disclosure statement filed April 19, 2005 (a duplicate of which was filed September 27, 2005) fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein (other than the US Patent cited therein) has not been considered. It is noted that the Form 903 mailed to applicant on May 23, 2008 did not reflect receipt of the references cited in the International Search Report. It is also noted,

however, that some of the references cited by applicant have been applied as prior art and have thus been cited on the PTO Form 892 included herewith.

Claim Objections

8. Claims 32-33 are objected to because of the following informalities. Claim 32 is incomplete, as the claim recites "wherein the cell is an". Claim 33 is improper because it is written such that it depends from itself. Appropriate correction is required.

In the interest of compact prosecution, claims 32-33 have been considered and interpreted as follows for examination purposes:

a) As the only cell type previously recited in claim 32 was an oocyte, the claim is interpreted as requiring that said cell is "an oocyte".

b) As claim 33 follows claim 32, the claim is interpreted as depending on claim 32.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-8 and 13-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-8 and 46-50 are indefinite because it is not clear how the claimed method achieves the stated objective of "determining the risk of reproductive failure in a

cell" (see text of independent claim 1). Particularly, the claims recite a final step of "comparing the measured length of the telomere to the standardized average length of a control telomere; to thereby determine the risk of reproductive failure in the cell." This recitation provides no indication as to how comparing telomere lengths actually relates to or results in determining risk of reproductive failure.

Claims 1-8 and 46-50 are indefinite over the recitation of the limitations "the chromosome" and "the measured length of the telomere" in claim 1. The claim does not previously refer to a single specific chromosome (but rather to "at least one chromosome") or to measurement of the length of a single particular telomere. Thus, it is not clear what is referenced by the limitations "the chromosome" and "the measured length of the telomere". (It is noted that dependent claims 4 and 46 also reference "the chromosome" and that dependent claim 7 references "the telomere"; accordingly, upon amending claim 1, applicant should also review the text of these claims to ensure that they clearly refer back to claim 1).

Claim 8 is indefinite because it is not clear how the claim further limits claim 1. Particularly, the claim merely requires the "method of claim 1 for use in *in vitro* fertilization (IVF)"; however, the language of the claim provides no indication as to how the method of claim 1 relates to or is involved in IVF. For example, what additional steps are performed when practicing the method of claim 8? Accordingly, the manner in which claim 8 actually further limits claim 1 is not clear.

Claims 13-18 are indefinite because it is not clear how the claimed method achieves the stated objective of "determining the predisposition of an oocyte to

reproductive failure" (see text of independent claim 13). Particularly, the claims recite a final step of "comparing the measured length of the telomere to the standardized average length of a control telomere; to thereby determine the predisposition of the oocyte to reproductive failure." This recitation provides no indication as to how comparing telomere lengths actually relates to or results in determining predisposition.

Claims 13-18 are indefinite over the recitation of the limitations "the chromosome" and "the measured length of the telomere" in claim 13. The claim does not previously refer to a single specific chromosome (but rather to "at least one chromosome") or to measurement of the length of a single particular telomere. Thus, it is not clear what is referenced by the limitations "the chromosome" and "the measured length of the telomere". (It is noted that dependent claim 14 also references "the chromosome" and that dependent claim 17 references "the telomere"; accordingly, upon amending claim 13, applicant should also review the text of these claims to ensure that they clearly refer back to claim 13).

Claims 19-23 are indefinite because it is not clear how the claimed method achieves the stated objective of "selecting a fertilized oocyte with a low risk of reproductive failure for *in vitro* fertilization" (see text of independent claim 19). Particularly, the claims recite a final step of "comparing the measured length of the telomere to the standardized average length of a control telomere; to thereby select a fertilized oocyte with a low risk of reproductive failure for *in vitro* fertilization". This recitation provides no indication as to how comparing telomere lengths actually relates to or results in selecting a fertilized oocyte with the required characteristics.

Claims 19-23 are indefinite over the recitation of the limitations "the chromosome" and "the measured length of the telomere" in claim 19. The claim does not previously refer to a single specific chromosome (but rather to "at least one chromosome") or to measurement of the length of a single particular telomere. Thus, it is not clear what is referenced by the limitations "the chromosome" and "the measured length of the telomere".

Claims 20-21 are indefinite over the recitation of the limitation "the subject" in claim 20. As the claims do not previously refer to a subject, there is insufficient antecedent basis for this limitation in the claims.

Claims 22-23 are indefinite over the recitation of the limitation "the subject" in claim 22. As the claims do not previously refer to a subject, there is insufficient antecedent basis for this limitation in the claims.

Claims 22-23 are indefinite because it is not clear whether the claims are drawn to a method "for optimizing the viability of an embryo," as stated in the preamble of claim 22, or to a method of selecting and implanting an oocyte, as suggested by the method steps of the claim. The language of the claim does not make clear how the step of implanting the oocyte actually relates to "optimizing the viability of an embryo."

Claims 24-33 are indefinite because it is not clear how the claimed method achieves the stated objective of "determining the risk of aneuploidy in a cell" (see text of independent claim 24). Particularly, the claims recite a final step of "comparing the measured length of the telomere to the standardized average length of a control telomere; to thereby determine the risk of aneuploidy in the cell". This recitation

provides no indication as to how comparing telomere lengths actually relates to or results in determining risk of aneuploidy.

Claims 24-33 are indefinite over the recitation of the limitations "the chromosome" and "the measured length of the telomere" in claim 24. The claim does not previously refer to a single specific chromosome (but rather to "at least one chromosome") or to measurement of the length of a single particular telomere. Thus, it is not clear what is referenced by the limitations "the chromosome" and "the measured length of the telomere". (It is noted that dependent claims 26 and 33 reference "the chromosome" and "said chromosome", respectively, and that dependent claim 29 references "the telomere"; accordingly, upon amending claim 24, applicant should also review the text of these claims to ensure that they clearly refer back to claim 24).

Claim 30 is indefinite because it is not clear how the claim further limits claim 26. Particularly, the claim merely requires the "method of claim 26 for use in *in vitro* fertilization (IVF)"; however, the language of the claim provides no indication as to how the method of claim 26 relates to or is involved in IVF. For example, what additional steps are performed when practicing the method of claim 30? Accordingly, the manner in which claim 30 actually further limits claim 26 is not clear.

Claims 31-33 are indefinite because it is not clear how the claims further limit claim 24. As claim 24 as written only employs a single cell, it is not clear how the recitation "said cell is in a population of cells" might further limit the claims. Further, it is not clear what might constitute a population of cells "representative of" a single cell, or

how the existence of such a population relates to or limits the claims. Clarification is required.

Claim 34 is indefinite because it is not clear how the claimed method achieves the stated objective of "selecting a fertilized oocyte with a low risk of aneuploidy for *in vitro* fertilization". Particularly, the claim recites a final step of "comparing the measured length of the telomere to the standardized average length of a control telomere; to thereby select a cell with a low risk of aneuploidy". This recitation provides no indication as to how comparing telomere lengths actually relates to or results in selecting a cell.

Claim 34 is indefinite over the recitation of the limitations "said chromosome" and "the chromosome" and "the measured length of the telomere". The claim does not previously refer to a single specific chromosome (but rather to "at least one chromosome") or to measurement of the length of a single particular telomere. Thus, it is not clear what is referenced by the limitations "the chromosome" and "the measured length of the telomere".

Claim 34 is also indefinite because it is unclear how the step of performing Q-FISH relates to the rest of the claim. The claim merely requires performing Q-FISH analysis; there is no indication as to what is actually being analyzed. Clarification is required.

Claims 35-41 are indefinite because it is not clear how the claimed method achieves the stated objective of "determining the predisposition of an oocyte to aneuploidy" (see text of independent claim 35). Particularly, the claims recite a final step of "comparing the measured length of the telomere to the standardized average

length of a control telomere; to optimize the viability of the embryo". This recitation provides no indication as to how comparing telomere lengths actually relates to or results in predisposition to aneuploidy. It is further noted that as claim 35 does not previously refer to an embryo, there is insufficient antecedent basis for the limitation "the embryo."

Claims 35-41 are indefinite over the recitation of the limitations "the chromosome" and "the measured length of the telomere" in claim 35. The claim does not previously refer to a single specific chromosome (but rather to "at least one chromosome") or to measurement of the length of a single particular telomere. Thus, it is not clear what is referenced by the limitations "the chromosome" and "the measured length of the telomere". (It is noted that dependent claim 36 also references "the chromosome" and that dependent claim 39 references "the telomere"; accordingly, upon amending claim 35, applicant should also review the text of these claims to ensure that they clearly refer back to claim 35).

Claim 40 is indefinite because it is not clear how the claim further limits claim 35. Particularly, the claim merely requires the "method of claim 35 for use in *in vitro* fertilization (IVF)"; however, the language of the claim provides no indication as to how the method of claim 35 relates to or is involved in IVF. For example, what additional steps are performed when practicing the method of claim 40? Accordingly, the manner in which claim 40 actually further limits claim 35 is not clear.

Claims 42-45 are indefinite because it is not clear how the claimed method achieves the stated objective of "pre-implantation genetic testing to identify an oocyte

with a predisposition to aneuploidy" (see text of independent claim 42). Particularly, the claims recite a final step of "comparing the measured length of the telomere to the standardized average length of a control telomere." This recitation provides no indication as to how comparing telomere lengths actually relates to or results in identifying an oocyte with a predisposition to aneuploidy.

Claims 42-45 are indefinite over the recitation of the limitations "the chromosome" and "the measured length of the telomere" in claim 42. The claim does not previously refer to a single specific chromosome (but rather to "at least one chromosome") or to measurement of the length of a single particular telomere. Thus, it is not clear what is referenced by the limitations "the chromosome" and "the measured length of the telomere". (It is noted that dependent claim 43 also references "the chromosome" and that dependent claim 44 references "the telomere"; accordingly, upon amending claim 42, applicant should also review the text of these claims to ensure that they clearly refer back to claim 42).

Claim 45 is indefinite because it is not clear how the claim further limits claim 42. Particularly, the claim merely requires the "method of claim 42 for use in *in vitro* fertilization (IVF)"; however, the language of the claim provides no indication as to how the method of claim 42 relates to or is involved in IVF. For example, what additional steps are performed when practicing the method of claim 45? Accordingly, the manner in which claim 45 actually further limits claim 42 is not clear.

Claim 48 is indefinite over the recitation of the limitation "nucleic acid sequence identified by any one of SEQ ID NOS: 1 through 10." Neither the specification nor the

prior art provide any kind of clear and limiting definition of the language "sequenced identified by," and it is not clear what types of relationships between a sequence and a SEQ ID NO are encompassed by this language. Accordingly, the types of sequences that are included and excluded by this claim language are not clear, and the metes and bounds of claim 48 are therefore unclear.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1, 4-5, 8, 24, 26-27, 30-31, and 46-47 are rejected under 35 U.S.C. 102(b) as being anticipated by Kozlowski et al (US 5,741,677 A [21 April 1998]).

Kozlowski et al disclose multiple rapid methods for measuring telomere lengths (see entire reference). The methods of Kozlowski et al comprise extracting genomic DNA comprising chromosomes, employing either PCR based or probe hybridization based techniques to determine telomere length, and comparing telomere length with standardized average length of a control telomere (according to a standard curve)(see entire reference, particularly col 3, line 1-col 5, line 53, Examples 1-2, and claim 2). Particularly, Kozlowski et al disclose that their methods may be used to diagnose cell senescence, "fertility problems", and infertility in males, noting that sperm cells from infertile males were found to have "significantly shorter telomeres" than sperm cells from fertile males (see col 5, lines 33-43 and claim 2). With regard to independent claim 1

and dependent claims, as infertility and "fertility problems" constitute conditions that inherently encompass a "risk of reproductive failure," and as Kozlowski et al disclose methods having all of the steps required by the claims, Kozlowski et al anticipate the claims. Regarding independent claim 24 and claims dependent therefrom, while the intended use of the method of claim 24 is "determining the risk of aneuploidy," the actual method steps of the claim merely require (as in claim 1) obtaining at least one chromosome, measuring telomere length, and comparing measured length with that of a standardized average length. The claim requires no manipulative steps in which "risk of aneuploidy" is actually determined. MPEP 2111.02 states that:

> If the body of a claim fully and intrinsically sets forth all of the limitations of the claimed invention, and the preamble merely states, for example, the purpose or intended use of the invention, rather than any distinct definition of any of the claimed invention's limitations, then the preamble is not considered a limitation and is of no significance to claim construction. *Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1165 (Fed. Cir. 1999).

Further, a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). In the instant case, as there is no manipulative difference between applicants' claimed method and that of Kozlowski et al, the recitation "for determining the risk of aneuploidy" is considered to constitute an intended use that is non-limiting for purposes of comparing the claimed invention to the prior art.

With further regard to dependent claims 4-5 and 26-27, Kozlowski et al disclose hybridizing an "oligonucleotide probe to a telomere repeat sequence, and determining the amount of probe hybridized as a measure of telomere length" (see, e.g., col 3, lines 58-62). Regarding claims 8 and 30, as the claim requires no additional method steps and as the method of Kozlowski et al could be employed for the intended use of IVF, the Kozlowski et al reference anticipates the claim. Regarding claim 31, it is noted, that, e.g., the sperm cells analyzed by the methods of Kozlowski et al are inherently representative of the sperm cells of the patients from which they were obtained. Regarding claim 46-47, Kozlowski et al disclose obtaining a labeled telomere-specific probe for use in their methods (see, e.g., col 4, lines 25-62).

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 6-7, 28-29, 33, and 48-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kozlowski et al (US 5,741,677 A [21 April 1998]) in view of Hultdin et al (Nucleic Acids Research 26(16):3651-3656 [August 1998]).

Kozlowski et al disclose multiple rapid methods for measuring telomere lengths (see entire reference). The methods of Kozlowski et al comprise extracting genomic DNA comprising chromosomes, employing either PCR based or probe hybridization based techniques to determine telomere length, and comparing telomere length with

standardized average length of a control telomere (according to a standard curve)(see entire reference, particularly col 3, line 1-col 5, line 53, Examples 1-2, and claim 2). Particularly, Kozlowski et al disclose that their methods may be used to diagnose cell senescence, "fertility problems", and infertility in males, noting that sperm cells from infertile males were found to have "significantly shorter telomeres" than sperm cells from fertile males (see col 5, lines 33-43 and claim 2).

Kozlowski et al do not disclose the use of a PNA-labeled probe as required by claims 6 and 28, or measurement of telomere length by Q-FISH, as required by claims 7, 29 and 33. Additionally, Kozlowski et al do not disclose the use of probes sharing identity with instant (elected) SEQ ID NO: 1, as required by claims 48-50.

Hultdin et al disclose a simple, rapid and reproducible Q-FISH method for measurement of telomere lengths (see entire reference, particularly the abstract and page 3655, right column). Hultdin et al's method employs a labeled PNA probe identical to instant SEQ ID NO: 1 (see, e.g., abstract and page 3652, left column). Hultdin et al teach that their method produces results within 30 hours (see abstract), i.e., a shorter time than the method of Kozlowski et al (note the teaching of three days to obtain results at col 5, lines 15-19 of Kozlowski et al). In view of the teachings of Hultdin et al, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Kozlowski et al so as to have employed the Q-FISH method and the probe of Hultdin et al in determining telomere lengths for comparison to achieve diagnosis of fertility problems and infertility as taught by Kozlowski et al. An ordinary artisan would have been motivated to have made such

a modification for the advantages of more rapid diagnosis, as well as the simplicity and high reproducibility of the assay, as explicitly taught by Hultdin et al.

With regard to claims 6-7 and 48-50, it is further noted that infertility and "fertility problems" constitute conditions that inherently encompass a "risk of reproductive failure." With further regard to claims 28-29 and 33, while the intended use of the method of the claims is "determining the risk of aneuploidy," the actual method steps of the claims merely require the steps suggested by the Kozlowski et al and Hultdin et al references. The claim requires no manipulative steps in which "risk of aneuploidy" is actually determined. MPEP 2111.02 states that:

> If the body of a claim fully and intrinsically sets forth all of the limitations of the claimed invention, and the preamble merely states, for example, the purpose or intended use of the invention, rather than any distinct definition of any of the claimed invention's limitations, then the preamble is not considered a limitation and is of no significance to claim construction. *Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1165 (Fed. Cir. 1999).

Further, a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). In the instant case, as there is no manipulative difference between applicants' claimed method and that suggested by Kozlowski et al in view of Hultdin et al, the recitation "for determining the risk of aneuploidy" is considered

to constitute an intended use that is non-limiting for purposes of comparing the claimed invention to the prior art.

15. Claims 2-3, 13-15, 18-23, 25, 32, 35-37, 40-43, and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kozlowski et al (US 5,741,677 A [21 April 1998]) in view of Kinugawa et al (Tohoku J. Exp. Med. 190:231-238 [2000]).

Kozlowski et al disclose multiple rapid methods for measuring telomere lengths (see entire reference). The methods of Kozlowski et al comprise extracting genomic DNA comprising chromosomes, employing either PCR based or probe hybridization based techniques to determine telomere length, and comparing telomere length with standardized average length of a control telomere (according to a standard curve)(see entire reference, particularly col 3, line 1-col 5, line 53, Examples 1-2, and claim 2). Particularly, Kozlowski et al disclose that their methods may be used to diagnose cell senescence, "fertility problems", and infertility in males, noting that sperm cells from infertile males were found to have "significantly shorter telomeres" than sperm cells from fertile males (see col 5, lines 33-43 and claim 2). However, Kozlowski et al do not disclose the practice of their methods on oocytes (either fertilized or unfertilized) or polar bodies therefrom.

Kinugawa et al disclose a comparison of telomerase activity in normal ovaries as compared to the ovaries of patients suffering from premature ovarian failure (POF), as well as telomerase activity in the ovaries of a population of younger women as compared to older women (see entire reference, particularly pages 232-235). Kinugawa et al teach that the enzyme telomerase is responsible for the lengthening of telomeres,

and that "telomere length shows the proliferative capacity remaining in cells" (page 232). Kinugawa et al report that telomerase activity decreases significantly with age (page 234), and further that POF subjects with follicle depletion also exhibited "very low telomerase activity" (page 234). Kinugawa et al conclude that their findings indicate that "telomerase activity decreases with the primordial follicle depletion that accompanies aging" (page 236) and that "Telomerase activity may be a useful marker of the ovarian functional age" (page 237).

In view of the teachings of Kinugawa et al, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Kozlowski et al so as to have practiced the method on either unfertilized or fertilized oocytes or polar bodies so as to have achieved a variety of different diagnostic objectives related to infertility or other potential fertility problems. Particularly, as Kozlowski et al disclose that telomeres are significantly shorter in germ cells from infertile males (sperm), and Kinugawa et al teach that activity of the enzyme responsible for telomere length decreases in the ovaries of older (and less fertile) females and POF patients with depleted follicles, the references suggest that telomere length can also be successfully measured in oocytes and polar bodies as an indicator of fertility or infertility, with significantly decreased telomere length relative to a normal (fertile) population serving as an indicator or risk factor for fertility problems.

With regard to claims 2-3, 13 and claims dependent therefrom, and 19 and claims dependent therefrom, it is further noted that infertility and "fertility problems" constitute conditions that inherently encompass a risk of or predisposition to

"reproductive failure." With further regard to claim 19 and claims dependent therefrom, it is also noted that as the combined references suggest that shorter telomeres are indicative of infertility, an ordinary artisan would have been motivated by the teachings of the references to have suggested fertilized oocytes or polar bodies therefrom having telomeres of a normal length for IVF so as to have increased the odds of a successful pregnancy. With further regard to claims 25, 32, 35-37, 40-43 and 45, and particular the intended uses recited therein, the actual method steps of the claims merely require the steps suggested by the Kozlowski et al and Kinugawa et al references. The claims requires no manipulative steps in which "risk of aneuploidy," "predisposition to aneuploidy," etc. is actually determined. MPEP 2111.02 states that:

> If the body of a claim fully and intrinsically sets forth all of the limitations of the claimed invention, and the preamble merely states, for example, the purpose or intended use of the invention, rather than any distinct definition of any of the claimed invention's limitations, then the preamble is not considered a limitation and is of no significance to claim construction. *Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1165 (Fed. Cir. 1999).

Further, a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). In the instant case, as there is no manipulative difference between applicants' claimed method and that suggested by Kozlowski et al in

view of Kinugawa et al, the intended use recitations in the claims are considered non-limiting for purposes of comparing the claimed invention to the prior art.

With further regard to dependent claims 14-15, 36-37, and 43, Kozlowski et al disclose hybridizing an "oligonucleotide probe to a telomere repeat sequence, and determining the amount of probe hybridized as a measure of telomere length" (see, e.g., col 3, lines 58-62). Regarding claims 40 and 45, as the claims require no additional method steps and as the method suggested by Kozlowski et al in view of Kinugawa et al could be employed for the intended use of IVF, the referenced suggest the claims. Regarding claim 18 and 41, it is noted, that, e.g., the sperm cells analyzed by the methods of Kozlowski et al are inherently representative of the sperm cells of the patients from which they were obtained, and that oocytes analyzed by the methods suggested by Kozlowski et al in view of Kinugawa et al would be similarly representative of oocytes from the patients from which they were obtained.

16. Claims 16-17, 33-34, 38-39, and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kozlowski et al in view of Kinugawa et al as applied to claims 2-3, 13-15, 18, 19-23, 25, 32, 35-37, 40-43, and 45, above, and further in view of Hultdin et al.

The teachings of Kozlowski et al and Kinugawa et al are set forth in the immediately preceding paragraph. Kozlowski et al and Kinugawa et al do not disclose the use of a PNA-labeled probe as required by claims 16 and 38, or measurement of telomere length by Q-FISH, as required by claims 17, 33-34, 39 and 44.

Hultdin et al disclose a simple, rapid and reproducible Q-FISH method for measurement of telomere lengths (see entire reference, particularly the abstract and

page 3655, right column). Hultdin et al's method employs a labeled PNA probe identical to instant SEQ ID NO: 1 (see, e.g., abstract and page 3652, left column). Hultdin et al teach that their method produces results within 30 hours (see abstract), i.e., a shorter time than the method of Kozlowski et al (note the teaching of three days to obtain results at col 5, lines 15-19 of Kozlowski et al). In view of the teachings of Hultdin et al, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Kozlowski et al in view of Kinugawa et al so as to have employed the Q-FISH method and the probe of Hultdin et al in determining telomere lengths. An ordinary artisan would have been motivated to have made such a modification for the advantages of more rapid diagnosis, as well as the simplicity and high reproducibility of the assay, as explicitly taught by Hultdin et al.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 571/272-0744. The examiner can normally be reached on Monday and Thursday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571/272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Diana B. Johannsen/
Primary Examiner, Art Unit 1634

Diana B. Johannsen
Primary Examiner
Art Unit 1634